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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/809,773 | 03/16/2001 | Frederick M. Ausubel | 00786/380002 | 8780 |

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| EXAMINER | |
|---|---|
| PRIEBE, SCOTT DAVID | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1632 | |

DATE MAILED: 03/22/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/809,773 | AUSUBEL ET AL. | |
| | Examiner | Art Unit | |
| | Scott D. Priebe, Ph.D. | 1632 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *27 January 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-25 and 27-48* is/are pending in the application.

4a) Of the above claim(s) *8-16,29 and 31-39* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,17-25,27,28,30 and 40-48* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *15 September 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

### *Continued Examination Under 37 CFR 1.114*

A request for continued examination under 37 CFR 1.114 was filed in this application after appeal to the Board of Patent Appeals and Interferences, but prior to a decision on the appeal. Since this application is eligible for continued examination under 37 CFR 1.114 and the fee set forth in 37 CFR 1.17(e) has been timely paid, the appeal has been withdrawn pursuant to 37 CFR 1.114 and prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on 1/27/05 has been entered.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

### *Drawings*

RRS

The petition to accept color drawings under 37 CFR 1.84 is granted.

RAM R. SHUKLA, PH.D.
SUPERVISORY PATENT EXAMINER

### *Claim Objections*

The numbering of claims is not in accordance with 37 CFR 1.126 which requires the original numbering of the claims to be preserved throughout the prosecution. When claims are canceled, the remaining claims must not be renumbered. When new claims are presented, they must be numbered consecutively beginning with the number next following the highest numbered claims previously presented (whether entered or not).

There are two sets of claims numbered 41, 42, and 43. The second set of these is misnumbered and should be renumbered as claims 44, 45 and 46, and the claims numbered 44 and 45 should be renumbered as claims 47 and 48.

Appropriate correction is required in response to this Office action. In anticipation of the renumbering of these claims by Applicant, the claims misnumbered as claims 41-45 are referred to below as claims 44-48.

***Claim Rejections - 35 USC § 112***

Claims 1-7, 17-25, 27, 28, 30 and 40-48 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1, 17 and 30 (and their dependent claims) have been amended to remove the limitation that the nematode be "persistently infected" with the bacterium and to add the limitation that the "bacterium increases ced programmed cell death in said nematode". Claims 40-48 recite that the "ced programmed cell death" is "ced-3", "ced-4", or "ced-9" programmed cell death. The added limitations pertaining to the bacterium increasing "ced programmed cell death in said nematode" is new matter with respect to the generic recitation of "bacterium", "nematode", and "ced," "ced-3," "ced-4," and "ced-9" "programmed cell death". Even if it were not new matter, the specification fails to provide an adequate written description of the genus of bacteria, nematode components of the combination required to produce a nematode infected with

a bacterium that produces generic ced programmed cell death or generic ced-3, -4, or –9 programmed cell death.

Applicant points to the specification at page 14, line 13, to page 20, line 6, as supporting the added limitation. However, this section of the specification describes the results of a working example were several different strains of the nematode *Caenorhabditis elegans,* specifically, are either infected specifically with the bacterium *Salmonella typhimurium* strain SL1344, infected specifically with the bacterium *Pseudomonas aeruginosa* strain PA14, or feeding on *Escherichia coli* strain OP50. The specification here discloses that infection of *C. elegans*, generically, by *S. typhimurium,* generically, but not by *P. aeruginosa*, generically, induces programmed cell death (PCD) specifically in the region of germ line cells occupied by syncytial germ cells undergoing meiosis and stained by SYTO 12 (p. 15, lines 1-4). The specification discloses that a deletion of phoP/phoQ/purB in the *S. typhimurium* abolishes induction of PCD in the *C. elegans* germline cells, but not killing by the infection (page 15). The specification discloses that ced-3, -4, and –9 and egl-1 are all involved in mediating the observed PCD (pp. 15-19), not just one of them without involvement of the remainder, as embraced by new claims 40-48. Finally, the specification here discloses that *P. aeruginosa* (pathogenic) and *E. coli* (food) do not elicit PCD in *C. elegans* feeding on them.

The specification does not disclose or describe a generic bacterium or generic *Salmonella* that induces generic ced, ced-3, ced-4, or ced-9 mediated PCD in a generic nematode. It does not mention, even in passing, that the description in the specification directed specifically to infection of *C. elegans* by *S. typhimurium* leading to PCD mediated by ced-3, ced-4, ced-9 and egl-1 extends to a generic bacterium or *Salmonella*, to a generic nematode, or to generic ced or

ced-3, ced-4, or ced-9 PCD. Consequently, there is evidence that Applicant had contemplated or was in possession of the generic invention presently being claimed. At most the specification describes an isolated *C. elegans* infected with *S. typhimurium*, which increases PCD specifically in germ line cells of the region occupied by syncytial germ cells undergoing meiosis and stained by SYTO 19, where the PCD is mediated by a pathway involving all of ced-3, ced-4, ced-9 and egl-1.

In addition to the issue of new matter, the specification does not adequately describe the generic invention being claimed. The claimed invention requires a combination of a bacterium and a nematode that upon infection of the nematode by the bacterium, PCD of at least some cells is increased. As indicated above the specification discloses only one such combination meeting the limitation of the claims, specifically *C. elegans* infected with *S. typhimurium*. The specification does not identify characteristics shared by nematodes that can be infected with bacteria that would induce ced PCD, nor does it identify characteristics shared by bacteria that would infect such nematodes and induce ced PCD.

With respect to a generic nematode, Bottjer et al. (Amer. J. Veterin. Res. 39 (1): 151-153, 1978) discloses that the parasitic nematode *Nematospiroides dubius* may be a carrier of *S. typhimurium* in nature. The success in growing infected *N. dubius* suggests that *N. dubius* is not harmed by *S. typhimurium*. Bottjer also discloses that parasitic helminths (roundworms) in general were known to be carriers of pathogenic Enterobacteriaceae, which appear to be pathogenic to *C. elegans*. Smerda et al. (J. Nematol. 3 (3): 201-204, July 1971) discloses that the free-living nematode *Pristionchus lheritieri* feed on salmonellae, which are pathogenic to humans but not the nematode. These results indicate that different nematodes react differently to

the same bacteria. With respect to a generic bacterium, the specification discloses that while *P. aeruginosa* is pathogenic to *C. elegans*, infection does not induce ced PCD. Smerda discloses that different species of *Salmonella, S. wichita* vs. *S. typhi*, give different results in terms of the frequency of nematodes fed the salmonellae that then defecate viable salmonellae. These results indicate that different pathogenic bacteria, and even different species of the same genus of bacteria, may differ in their interaction with the same nematode. Consequently, the finding that a specific species of bacteria produces a particular result upon interaction with a specific species of nematode, does not suggest that other combinations of bacteria and nematodes will produce the same result.

One cannot envision, based upon the specification, the particular combinations of nematode and bacterium, other than *C. elegans* and *S. typhimurium*, that would produce the infected nematode required by the claimed invention, because of the lack of sufficient numbers of disclosed species and the lack of disclosed characteristics that would allow one to recognize particular combinations of bacterium and nematode as being embraced by the invention. The prior art shows that different nematodes interact with different bacteria in different ways. Therefore, one of skill in this art would not accept that Applicant was in possession or had described the genus of infected nematode to which the claims are directed based solely upon the disclosure of one specific combination of nematode and bacterium that meets the requirements of the invention.

Claims 1-7, 17-25, 27, 28, 30 and 40-48 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated *C. elegans* infected with *S.*

*typhimurium* resulting in increased PCD of germ line cells in the region occupied by syncytial germ cells undergoing meiosis and stained by SYTO 12 that is mediated by ced-3, ced-4, ced-9 and egl-1, does not reasonably provide enablement for any other combination of nematode and bacterium or type of ced PCD. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

The claims are broadly directed to any nematode infected with any bacterium such that the bacterium causes an increase in ced PCD.

The grounds of rejection set forth in the preceding rejection are incorporated here. To summarize, the specification discloses only one species readable on the invention - *C. elegans* infected with *S. typhimurium* which induces increased PCD specifically of germ line cells in the region occupied by syncytial germ cells undergoing meiosis and stained by SYTO 12 that is mediated by ced-3, ced-4, ced-9 and egl-1. The specification does not provide any guidance as to what characteristics a suitable bacterium must possess or what characteristics a suitable nematode must possess that when in combination result in increased ced PCD in general. Neither does it provide guidance as to combinations of a bacterium and a nematode that would result in PCD in cells other than germ line cells in the region occupied by syncytial germ cells undergoing meiosis and stained by SYTO 12 or that involves host genes other than all of ced-3, ced-4, ced-9 and egl-1. Both the specification and the prior art show that different bacteria interact differently with different nematodes. Thus one cannot predict any specific combination of bacteria and nematode that meets the limitations of the claims and commensurate in scope with the breadth of the claims.

As set forth in In re Fisher, 166 USPQ 18, 24 (CCPA 1970), compliance with 35 USC 112, first paragraph requires:

> that scope of claims must bear a reasonable correlation to scope of enablement provided by specification to persons of ordinary skill in the art; in cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific laws; in cases involving unpredictable factors, such as most chemical reactions and physiological activity, scope of enablement varies inversely with degree of unpredictability of factors involved.

A patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion. Tossing out the germ of an idea does not constitute an enabling disclosure. While every aspect of a generic claim need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable the skilled artisan to understand and carry out the invention. It is true that a specification need not disclose what is well known in the art. However, that general, oft-repeated statement is merely a rule of supplementation, not a substitute for a basic enabling disclosure. It means that the omission of minor details does not cause a specification to fail to meet the enablement requirement under 35 USC 112, first paragraph. When there is no disclosure of the specific starting materials or conditions under which the process can be carried out, there is a failure to meet the enablement requirement. See *Genentech Inc. v. Novo Nordisk A/S*, 42 USPQ2d 1001, 1005 (Fed. Cir. 1997). What is lacking is the disclosure of specific starting materials commensurate in scope with the application.

In order to practice the invention as broadly as is claimed, one would have to resort to unguided trial and error experimentation to identify other specific combinations of a bacterium and nematode that satisfy the limitations of the claims. Such experimentation is undue.

Applicant's arguments filed 1/27/05 have been fully considered but they are not persuasive for the reasons set forth above. The simplicity or complexity of what would be required in order to carry out the unguided trial and error experimentation is not germane. What is germane is that unguided trial and error experimentation would be required, and such experimentation is undue.

Claims 17-25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 17 recites "determining whether the test compound inhibits said bacterium in said infected nematode." It is unclear what "inhibits said bacterium" means in this context, or in what way the bacterium is being inhibited. To inhibit generally refers to a process or action, but the process or action is not identified by the claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Scott D. Priebe, Ph.D. whose telephone number is (571) 272-0733. The examiner can normally be reached on M-F, 8:00-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Scott D. Priebe, Ph.D.
Primary Examiner
Art Unit 1632

Scott D. Priebe